Natural history of carotid artery occlusion contralateral to carotid endarterectomy

Ali F. AbuRahma, MD, Patrick A. Stone, MD, Shadi Abu-Halimah, MD, and **Christine A. Welch, MS,**
Charleston, WV

Background: **The natural history of patients with carotid artery occlusion is controversial. A few studies have concluded that patients with internal carotid artery occlusion carry a high risk of neurologic events. None of these previously reported studies analyze the natural history of internal artery occlusion contralateral to carotid endarterectomy (CEA), except for a small series including a subset of patients from two randomized trials, the Asymptomatic Carotid Atherosclerosis Study and the North American Symptomatic Carotid Endarterectomy Trial. This study analyzes the natural history of patients with carotid artery occlusion contralateral to CEA, specifically assessing long-term neurologic events occurring in the hemisphere associated with the occluded carotid artery.**

Methods: **Of the 599 CEAs in 544 patients that were included in two previously updated prospective studies, 63 patients had contralateral internal carotid artery occlusion, and their perioperative and long-term outcomes were evaluated. A Kaplan-Meier analysis was used to estimate the rate of freedom from late stroke occurring in the hemisphere ipsilateral to the occluded carotid artery. The stroke-free survival rate was also noted.**

Results: **Mean follow-up was 58 months (range, 1 to 147 months). One perioperative stroke (1.6%) occurred, which was not in the cerebral hemisphere ipsilateral to the occluded carotid artery. Two late strokes (3.2%) and nine transient ischemic attacks (TIAs) (14.3%) occurred involving the hemisphere of the occluded carotid artery. There were also three late TIAs (4.8%) and no late strokes involving the hemisphere supplied by the operative site. There were a total of 14 late deaths. Fifteen patients had late ≥50% restenosis of the operative side. Six of these had neurologic events (TIA/stroke) involving the hemisphere of the occluded carotid artery, in contrast to five of 48 patients with no restenosis who had neurologic symptoms ($P < .001$). Freedom from late strokes in the hemisphere ipsilateral to the occluded carotid artery at 1, 3, 5, and 10 years was 98%, 96%, 96%, and 96%, respectively. The stroke-free survival rates at 1, 3, 5, and 10 years were 90%, 87%, 80%, and 59%, respectively.**

Conclusions: **The natural history of carotid artery occlusion contralateral to CEA is relatively benign. This may suggest a protective effect of carotid endarterectomy on the cerebral hemisphere ipsilateral to the carotid occlusion from late strokes. (J Vasc Surg 2006;44:62-6.)**

The natural history of patients with carotid artery occlusion is controversial. It is generally thought that internal carotid artery (ICA) occlusion initially correlates with potentially serious neurologic events; however, once the occlusion is established, the incidence of subsequent neurologic events seems to be lower.[1-6] Nicholls et al[4] concluded that when ICA occlusion occurs, patients have an initial risk of ipsilateral stroke that can be as high as 25%. The subsequent risk of stroke ipsilateral to the occlusion appears to vary according to its initial clinical presentation, with the incidence of stroke reported to range from 0% to 5% annually in patients with asymptomatic occlusions[6,7] to as high as 27% in patients with symptomatic occlusions.[1,2]

Few previously reported studies have analyzed the natural history of ICA occlusion contralateral to carotid endarterectomy (CEA).[8-10] This study analyzes the natural history of patients with carotid artery occlusion contralateral to CEA, specifically assessing long-term neurologic events occurring in the hemisphere associated with the occluded carotid artery.

From the Department of Surgery, Robert C. Byrd Health Sciences Center, West Virginia University.

Competition of interest: none.

Presented at the Thirtieth Annual Meeting of the Southern Association for Vascular Surgery, Phoenix, Ariz, Jan 18-21, 2006.

Correspondence: Ali F. AbuRahma, MD, 3110 MacCorkle Avenue, SE, Charleston, WV 25304 (e-mail: ali.aburahma@camc.org).

0741-5214/$32.00

doi:10.1016/j.jvs.2006.03.010

METHODS

Of 599 CEAs in 544 patients that were included in two previous prospective trials, 63 patients had contralateral ICA occlusion.[11,12] This study will only analyze the natural history of those patients with contralateral carotid artery occlusion. The Institutional Review Board of our institution approved the study. Details of the two prospective trials were described previously.[11,12]

Before surgery, all patients underwent carotid color duplex ultrasound scanning or magnetic resonance angiography (MRA), or both, to determine preoperative stenosis. Various preoperative risk factors were determined, including hypertension, diabetes mellitus, smoking, coronary artery disease, and the preoperative use of antiplatelet therapy.

All CEAs were done under general anesthesia, and routine shunting was used. All patients were administered aspirin therapy (325 mg daily) ≤24 hours after the operation or Plavix (75 mg daily) (Bristol-Myers Squibb, New York, NY) if aspirin was contraindicated. Eighty-three percent of these patients had preoperative antiplatelet therapy.

The diagnosis of ICA occlusion was accomplished by duplex ultrasound imaging with or without MRA. Ultra-

Table I. Demographic and clinical characteristics

Characteristic	*Number (%)**
Sex	
Male	44 (70)
Female	19 (30)
Age, mean (range)	66.54 (41–88)
Hypertension	46 (73)
Diabetes mellitus	18 (29)
Hyperlipidemia	33 (52)
Smoking	43 (68)
Coronary artery disease	31 (49)
Indications for surgery	
Hemispheric TIA	14 (22)
Hemispheric stroke	15 (24)
Amaurosis fugax	5 (8)
Nonhemispheric	14 (22)
TIA	
Asymptomatic	15 (24)

TIA, Transient ischemic attack.
*All data are number (%) except for age, which is mean (range).

Table II. Perioperative complications

Complication	*Number (%)*
TIA (operative side)	1 (1.6)*
Stroke (operative side)	1 (1.6)†
Stroke (ipsilateral to carotid occlusion)	0
Myocardial infarction	1 (1.6)
Congestive heart failure	1 (1.6)
Death	1 (1.6)

TIA, Transient ischemic attack.
*This patient had carotid endarterectomy with Hemashield (Boston Scientific, Natick, Mass) patching.
†This patient had carotid endarterectomy with primary closure.

Table III. Late neurologic events and death

Event	*Number (%)*
TIA (operative side)	3 (4.8)*
TIA (ipsilateral to carotid occlusion)	9 (14.3)†
Stroke (ipsilateral to carotid occlusion)	2 (3.2)‡
Death	14 (22.2)
Myocardial infarction	6
Congestive heart failure	1
Respiratory failure	1
Renal failure	1
Sepsis	1
Suicide	1
Cancer	1
Unknown	2

TIA, Transient ischemic attack.
*Two patients had primary closure, and one patient had a Hemashield patch.
†Three patients had primary closure and six patients had patching (four Hemashield patches and two polytetrafluoroethylene).
‡One patient had primary closure and one had Hemashield patching.

sound criteria for ICA occlusion included the lack of color flow in the ICA, detection of a diastolic flow towards zero in the common carotid artery, and a clear demonstration of an external carotid artery and its collaterals. In patients with suboptimal duplex imaging, MRA was done to confirm carotid artery occlusion.

Postoperative surveillance protocol. All patients had clinical and neurologic examinations postoperatively and underwent immediate postoperative color duplex ultrasound scanning of the operated side, which was repeated at 30 days, 6 months, and every 6 months thereafter using an ATL/HDI system 3000 and 5000 (Advanced Technology Laboratory, Inc., Seattle, Was). Reportable complications were determined in accordance with the Society of Vascular Surgery Ad Hoc Committee Suggested Standards for Reports Dealing with Cerebrovascular Disease.[13] All patients with early and late postoperative neurologic events were examined clinically (including neurologic consultations) and had computed tomography scanning or magnetic resonance imaging of the brain. They also had a carotid duplex ultrasound and cardiac evaluation if the source of emboli was not clear.

Statistical analysis. Kaplan-Meier life-table analysis was used to calculate freedom from late strokes in the hemisphere ipsilateral to the carotid occlusion. The stroke-free survival rates were also calculated. Discrete variables were compared using Fisher's exact test.

RESULTS

As noted, 63 patients were in this study. The follow-up was 58 months (range, 1 to 147 months). Table I summarizes the demographic and clinical characteristics of this series. The patients' initial presentations included 14 (22%) with hemispheric transient ischemic attacks (TIAs), 15 (24%) with hemispheric strokes, 5 (8%) with amaurosis fugax, 14 (22%) with nonhemispheric TIAs, and 15 (24%) were asymptomatic. The perioperative complications are summarized in Table II. As noted, one stroke (1.6%) occurred on the operative side, and no strokes were ipsilateral to the carotid occlusion.

The late neurologic events (TIAs and strokes) and deaths are summarized in Table III. Two late strokes (3.2%) occurred in the hemisphere ipsilateral to the occluded artery, one of which was similar to one that occurred 2 years before the CEA. The other patient had a prior asymptomatic carotid occlusion. One of these patients had a complete neurologic recovery. Nine late TIAs (14.3%) occurred in the hemisphere ipsilateral to the carotid occlusion. Five of these were similar to previous TIAs, and four others were new transient ischemic events. All of these patients were treated with antiplatelet therapy, except for two patients who were treated with anticoagulation therapy because of cardiac arrhythmias. There were also three (4.8%) late TIAs but no late strokes involving the operative side.

Of the two patients with strokes in the hemisphere ipsilateral to the occluded carotid, one was associated with ≥50% restenosis of the operated side, and the other patient demonstrated no recurrent stenosis. Five of the nine TIAs involving the hemisphere ipsilateral to the occluded carotid were associated with ≥50% restenosis at the CEA site, and

Table IV. Freedom from late strokes (ipsilateral to carotid occlusion)

Time interval risk (mos.)	*No. at risk at start*	*No. failed*	*No. withdrawn*	*Interval survival*	*Cumulative contralateral stroke-free*	*SE*
0-<1	63	0	1	100	100	0
1-6	62	0	5	100	100	0
6-12	57	1	1	98.23	98.23	1.75
12-18	55	0	1	100	98.23	1.75
18-24	54	1	3	98.1	96.36	2.53
24-30	50	0	1	100	96.36	2.53
30-36	49	0	3	100	96.36	2.53
36-42	46	0	4	100	96.36	2.53
42-48	42	0	6	100	96.36	2.53
48-54	36	0	4	100	96.36	2.53
54-60	32	0	6	100	96.36	2.53
60-72	26	0	9	100	96.36	2.53
72-84	17	0	1	100	96.36	2.53
84-96	16	0	3	100	96.36	2.53
96-108	13	0	3	100	96.36	2.53
108-120	10	0	4	100	96.36	2.53
120-132	6	0	2	100	96.36	2.53
132-144	4	0	0	100	96.36	2.53
144-156	4	0	4	100	96.36	2.53

SE, Standard error.

four were associated with normal to <50% stenosis at the CEA site. Overall, 15 patients in the group had late ≥50% restenosis, 10 of which had primary closure (only three of these were ≥70%). Six of these restenosis were associated with neurologic events (TIA or stroke) in the hemisphere ipsilateral to the occluded carotid, in contrast to five of 48 patients with no restenosis who had neurologic events ($P <$ .001).

Table IV summarizes the life-table analysis of freedom from late strokes in the hemisphere ipsilateral to the carotid occlusion (Fig 1). The freedom from stroke at 1, 3, 5, and 10 years was 98.2%, 96.4%, 96.4%, and 96.4%, respectively. A total of 14 late deaths were caused by six myocardial infarctions, one each from congestive heart failure, respiratory failure, renal failure, sepsis, suicide, and malignancy, and two from an unknown cause. The stroke-free survival rates are summarized in Table V and Fig 2. The stroke-free survival rate at 1, 3, 5, and 10 years was 90.3%, 86.9%, 80.2%, and 58.8%, respectively.

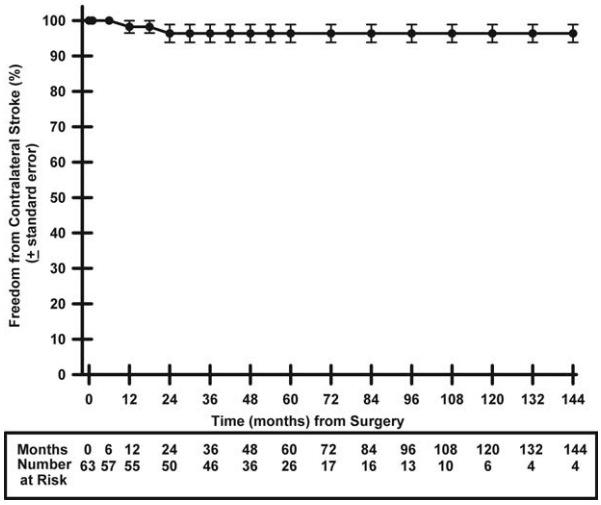

Fig 1. Kaplan-Meier life-table analysis of freedom from late strokes (ipsilateral to the carotid occlusion).

DISCUSSION

Occlusion of the ICA represents end-stage disease of the involved vessel. This potentially stroke-inducing event can be prevented by CEA. Roederer et al[14] found that individuals at high risk for progression to occlusion have >80% diameter reduction of the ICA. Once the carotid artery is occluded, an annual stroke rate of 3% can be anticipated, with two thirds of events involving the ipsilateral territory.[15] Outcome appears to depend on the initial neurologic presentation. Patients presenting with carotid occlusion and hemispheric infarction have a fourfold increase in the incidence of having a second hemispheric stroke compared with patients whose initial presentation is a TIA.[16] Additionally, the risk of subsequent stroke in patients with asymptomatic occlusion approaches 11%, resulting in a stroke-free rate of 89% at 4 years compared with 67% for symptomatic occlusions.[15] In contrast, only two late strokes in the hemisphere ipsilateral to the carotid occlusion were noted in our series, resulting in a 96% stroke-free rate at 5 years.

Other authors have suggested that the natural history of the patent ICA contralateral to carotid occlusion is different than in individuals without carotid occlusion. Brengman et al[17] looked specifically at the rate of disease progression in the patent ICA by duplex examination and the eventual need for CEA in patients with contralateral carotid occlusion. Disease progression and the need for subsequent CEA was 85% at 8 years in their series, and they recommended frequent follow-up for a longer duration in this population because disease appeared to progress over a short duration.[17]

Table V. Stroke-free survival

Time interval (mos.)	*No. at risk at start*	*No. failed*	*No. withdrawn*	*Interval survival*	*Cumulative contralateral stroke-free*	*SE*
0–<1	63	1	0	98.41	98.41	1.57
1–6	62	3	2	95.08	93.57	3.11
6–12	57	2	0	96.49	90.29	3.77
12–18	55	0	1	100	90.29	3.77
18–24	54	2	2	96.23	86.88	4.33
24–30	50	0	1	100	86.88	4.33
30–36	49	0	3	100	86.88	4.33
36–42	46	0	4	100	86.88	4.33
42–48	42	2	4	95	82.54	5.09
48–54	36	1	3	97.1	80.15	5.47
54–60	32	0	6	100	80.15	5.47
60–72	26	1	8	95.45	76.50	6.32
72–84	17	0	1	100	76.50	6.32
84–96	16	2	1	87.1	66.63	8.53
96–108	13	0	3	100	66.63	8.53
108–120	10	1	3	88.24	58.79	10.53
120–132	6	1	1	81.82	48.10	12.95
132–144	4	0	0	100	48.10	12.95
144–156	4	0	4	100	48.10	12.95

SE, Standard error.

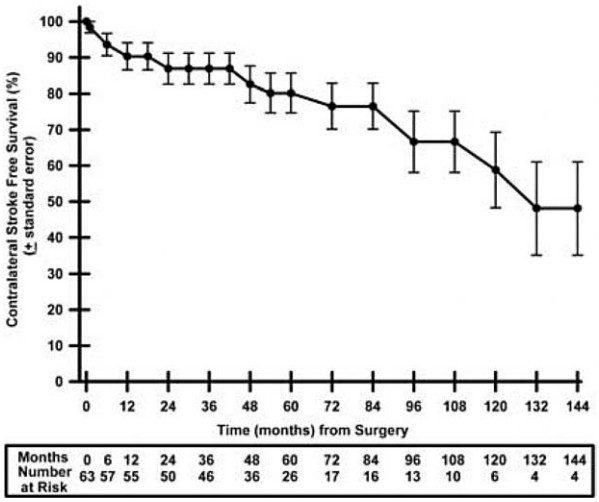

Fig 2. Kaplan-Meier life-table analysis of stroke-free survival rates.

Concern has been expressed that the risk of perioperative stroke is increased during CEA when the contralateral ICA is occluded.[18] Before 1980, perioperative stroke rates of 11% and 13% were reported by Anderson et al[19] and Chung.[20] However, more recent work by Mackey et al[21] has demonstrated respective stroke rates of 4.8% and 2.6% in their patients with contralateral occlusion. Ballotta et al[22] evaluated presumed high-risk octogenarians with and without contralateral carotid occlusion who completed CEA, comparing the outcomes with younger groups of similarly matched patients. Outcome differences among age groups did not exist with respect to age or to severity of contralateral occlusive disease.[22] This updated version of our experience with ICA occlusion indicates that CEA does not result in an increased risk of perioperative strokes or TIAs, irrespective of contralateral ICA patency.[23]

Is there then a protective effect for the cerebral hemisphere ipsilateral to the carotid occlusion with contralateral CEA? Mackey et al[21] reported a 5-year cumulative stroke rate of only 2% in patients with an occluded carotid after contralateral CEA. Nicholls et al[15] reported a 5-year cumulative stroke rate of 11% in patients who had CEA, compared with a 22% cumulative stroke rate for those who did require CEA contralateral to the occlusion. Similarly, in our series, only two late (3.2%) strokes occurred in the hemisphere ipsilateral to the carotid occlusion, which may suggest that contralateral CEA may provide a protective effect for the hemisphere ipsilateral to the occlusion. In addition, patients with recurrent stenosis after CEA were at an increased risk of late neurologic events in the hemisphere ipsilateral to the occluded artery. Indeed, neurologic events (TIA/stroke) developed in 40% of patients with >50% restenosis vs 10% in patients without recurrent disease after CEA ($P < .001$).

Finally, 5-year survival among patients with carotid occlusion has been reported at 63% to 77%.[16,24] Stroke-free survival in our series was similar, with a survival rate of 80% at 5 years and 59% at 10 years. Cardiac-related events accounted for 50% of deaths in our series. These findings were comparable with previously published reports.[4,15]

CONCLUSION

Thus, based on review of our prospective database, we conclude that CEA contralateral to a carotid occlusion can be performed with acceptable perioperative morbidity and mortality rates. Additionally, the natural history of carotid artery occlusion contralateral to CEA appears more benign than what was previously reported for similar patients *not* undergoing CEA. Likewise, patients with recurrent steno-

sis after contralateral CEA experienced more neurologic events ipsilateral to the occluded artery than those free from restenosis. This suggests an overall protective effect in the hemisphere ipsilateral to the carotid occlusion from late stroke when CEA is performed for occlusive disease of the contralateral ICA.

AUTHOR CONTRIBUTIONS

Conception and design: AFA
Analysis and interpretation: AFA, PAS
Data collection: SAH
Writing the article: AFA, PAS, SAH
Critical revision of the article: AFA
Final approval of the article: AFA, PAS, SAH, CAW
Statistical analysis: CAW
Obtained funding: Not applicable
Overall responsibility: AFA

REFERENCES

1. Cote R, Barnett HJM, Taylor DW. Internal carotid occlusion: a prospective study. Stroke 1983;14:898-902.
2. Persson AV, Griffey EE. The natural history of total occlusion of the internal carotid artery. Surg Clin North Am 1985;65:411-16.
3. Pierce GE, Keushkerian SM, Hermreck AS, Iliopoulos JI, Thomas JH. The risk of stroke with occlusion of the internal carotid artery. J Vasc Surg 1988;8:74-80.
4. Nicholls SC, Bergelin R, Strandness DE. Neurologic sequelae of unilateral carotid artery occlusion: immediate and late. J Vasc Surg 1989; 10:542-8.
5. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. Endarterectomy for asymptomatic carotid stenosis. JAMA 1995; 273:1421-8.
6. Bornstein NM, Norris JW. Benign outcome of carotid occlusion. Neurology 1989;39:6-8.
7. Hennerici M, Hulsbomer HB, Rautenberg W, Hefter H. Spontaneous history of asymptomatic internal carotid occlusion. Stroke 1986;17: 718-22.
8. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. Endarterectomy for asymptomatic carotid artery stenosis. JAMA 1995;278:1421-28.
9. North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade stenosis. N Engl J Med 1991;325:445-53.
10. Jacobwitz GR, Adelman MA, Riles ?? Ts, Lamparello PJ, Imparato AM. Long-term follow-up of patients undergoing carotid endarterectomy in the presence of a contralateral occlusion. Am J Surg 1995;170:165-7.
11. AbuRahma AF, Robinson PA, Saiedy S, Khan JH, Boland JP. Prospective randomized trial of carotid endarterectomy with primary closure and patch angioplasty with saphenous vein, jugular vein, and polytetrafluoroethylene: Longterm follow-up. J Vasc Surg 1998;27:222-34.
12. AbuRahma AF, Hopkins ES, Robinson PA, Deel JT, Agarwal S. Prospective randomized trial of carotid endarterectomy with polytetrafluoroethylene versus collagen-impregnated Dacron (Hemashield) patching: late follow-up. Ann Surg 2003;237:885-92.
13. Baker JD, Rutherford RB, Bernstein EF, Courbier R, Ernst CB, Kempczinski RF, et al. Suggested standards for reports dealing with cerebrovascular disease. J Vasc Surg 1988;8:721-9.
14. Roederer GO, Langlois YE, Jager KA, Primozich JF, Beach KW, Phillips DJ, et al. The natural history of carotid arterial disease in asymptomatic patients with cervical bruits. Stroke 1984;15:605-13.
15. Nicholls SC, Kohler TR, Bergelin RO, Primozich JF, Lawrence RL, Strandness DE. Carotid artery occlusion: natural history. J Vasc Surg 1986;4:479-85.
16. Faught WE, van Bemmelen PS, Mattos MA, Hodgson KJ, Barkmeier LD, Ramsey DE, et al. Presentation and natural history of internal carotid artery occlusion. J Vasc Surg 1993;18:512-23.
17. Brengman ML, O'Donnell SD, Mullenix P, Goff JM, Gillespie DL, Rich NM. The fate of a patent carotid artery contralateral to an occlusion. Ann Vasc Surg 2000;14:77-81.
18. Fields WS, Lamak N. Joint study of extracranial arterial occlusion. JAMA 1976;235:2734-8.
19. Anderson CA, Rich NM, Collins GJ, McDonald PT, Boone SC. Unilateral internal carotid occlusion: special considerations. Stroke 1977;8: 669-71.
20. Chung WB. Long-term results of carotid artery surgery for cerebrovascular insufficiency. Am J Surg 1974;128:262-8.
21. Mackey WC, O'Donnell TF, Callow AD. Carotid endarterectomy contralateral to an occluded artery: perioperative risk and late risk. J Vasc Surg 1990;11:778-85.
22. Ballotta E, Renon L, Da Giau G, Barbon B, Terranova O, Baracchini C. Octogenarians with contralateral carotid artery occlusion: a cohort at higher risk for carotid endarterectomy? J Vasc Surg 2004;39:1003-08.
23. AbuRahma AF, Robinson P, Holt SM, Herzog TA, Mowery NT. Perioperative and late stroke rates of carotid endarterectomy contralateral to carotid artery occlusion. Stroke 2000;31:1566-71.
24. Furlan AJ, Whisnant JP, Baker HL. Long-term prognosis and carotid artery occlusion. Neurology 1980;30:986-8.

Submitted Nov 8, 2005; accepted Mar 2, 2006.